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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,648	10/05/2000	Mark F. Charette	CIBT-P01-569	7787

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EXAMINER	
BALLARD, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 03/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,648	CHARETTE ET AL.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/27/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8,11,12,16-19,22,25,26 and 33-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,11,12,16-19,22,25,26 and 33-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 December 2005 has been entered.

The Examiner of U.S. Patent Application No. 09/509,648 has changed. In order to expedite the correlation of papers with the application, please direct all future correspondence to Examiner Ballard, Technology Center 1600, Art Unit 1649.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The amendment of 27 December 2005 has been entered in full. Claims 1-2, 18, 35 and 38 have been amended. Claims 3-4, 9-10, 13-15, 20-21, 23-24, and 27-32 have been cancelled. Claims 39-41 have been added.

Claims **1-2, 5-8, 11-12, 16-19, 22, 25-26,** and **33-41** are under consideration in the instant action. The claims also read upon the following species: Alzheimer's disease from the disorder group, cytokine antagonist from the agent capable of releasing morphogen activity group, (2-p-bromocynnamylaminoethyl)-5-isoquinolinesulfonamide from the protein kinase A inhibitor group, SEQ ID NO: 2 from

the morphogen amino acid sequence group, OP-1 from the morphogen group, and retinoid receptor from the molecule that binds an endogenous ligand group.

Withdrawn Objections and/or Rejections

The objection to claims 35 and 38 for use of the acronyms "OP-1" and "CNTF" as set forth at page 15 ¶41 of the previous office action (mailed 13 May 2005) is *withdrawn* in view of Applicant's amendments to the claims.

The rejection of claims 23-24 under 35 U.S.C. 112, first paragraph (Enablement), as set forth at pages 4-10 of the previous office action (mailed 13 May 2005) is moot in view of Applicant's cancellation of said claims (filed 27 December 2005).

The rejection of claims 23-24 under 35 U.S.C. 112, first paragraph (Written Description), as set forth at pages 10-13 of the previous office action (mailed 13 May 2005) is moot in view of Applicant's cancellation of said claims (filed 27 December 2005).

The rejection of claims 1, 5, 6, 8, 11, 12, 19, 22, 25, 26, 33-35, 37 and 38 under 35 U.S.C. 112, second paragraph, as set forth at page 14 of the previous office action (13 May 2005) as being indefinite for the term "morphogen activity" is hereby *withdrawn* in view of Applicant's amendments to the claims.

The rejection of claim 12 under 35 U.S.C. 112, first paragraph (written description), as set forth at pages 10-13 of the previous office action (13 May 2005) is hereby *withdrawn* upon further consideration.

Maintained Objections and/or Rejections

Specification

The disclosure is objected to because of the following informalities: Patent applications are referenced in the disclosure (p. 25, line 25). The basis for this objection is set forth at page 3-4 of the office action of 27 August 2003, at page 3 of the office action of 26 July 2004, and at pages 3-4 of the Office action of 13 May 2005. The Examiner acknowledges that the application cited therein is still pending and notes Applicant's intention to make the necessary amendments.

Claim Objections

The objections to claims 8, 11, 16-17, 19, 22, and 26 as noted at page 4 ¶12 in the previous office action of 13 May 2005 regarding the issue that the claims are not limited to the elected species are maintained and held in abeyance until allowable subject matter is identified.

Claim Rejections - 35 USC § 112, 1st Paragraph

The rejection of claims 1-2, 5-8, 11-12, 16-19, 22, 25-26, 33-38 under 35 U.S.C. 112, first paragraph (scope), is maintained for reasons set forth at pages 4-10 of the

previous office action of 13 May 2003 and at pages 4-15 of the office action of 26 July 2004, and is applied to new claim 39 as it pertains to a method of influencing neuronal proliferation, growth, and maintenance in the differentiated state *in vitro*. The specification, while being enabling for a method of reducing leukemia inhibitory factor (LIF)-induced dendritic retraction comprising adding an antibody against gp130 to sympathetic neurons *in vitro* that have been treated with LIF and osteogenic protein-1 (OP-1) and wherein said antibody reduces LIF-induced dendritic retraction, *does not* reasonably provide enablement for a method for promoting neuronal cell growth, a method for influencing neuronal proliferation, growth, and maintenance in the differentiated state, or a method of promoting neuronal cell growth or increasing neuronal proliferation, growth, and maintenance in the differentiated state in a neuron injured by a neurodegenerative disorder *in vitro or in vivo*.

Applicant's arguments filed 27 December 2005 as they pertain to the rejection have been fully considered but they are not persuasive.

Applicants assert that the specification adequately enables the full scope of the invention. Applicants state that the identity of the morphogen that is exhibiting the observed activity is not necessary to practice he claimed invention. Applicants assert that there are means known in the art to identify morphogens if need be, and futher that any morphogen described in the specification is appropriate, as supported by art describing the overlap of morphogen activity (Exhibits A and B). While the examiner concedes that while any morphogen may be sufficient to practice claims 6 and 7, for

example, the specification, however, does not provide sufficient guidance to practice the invention within the full scope of the claims.

The amended limitations of claims 1 and 2 do not negate the previous office action's assertion that the specification is lacking on guidance to enable the artisan to understand and carry out the invention in its full scope. It is noted that the claims still read on *in vivo* methods of reducing inhibition of a morphogen activity in a neuron or for promoting neuronal cell growth. The limitations "which reduces inhibition of the morphogen activity in the neuron *in vitro*" (claim 1) and "which overcomes inhibition of growth-promoting effects of endogenous morphogens *in vitro*" (claim 2) are inherent properties of the agent being applied, and do not limit the "method for reducing inhibition of a morphogen" or the "method for promoting neuronal cell growth" to *in vitro* methods.

Applicant has provided little or no guidance beyond *in vitro* data that would enable one of ordinary skill in the art to determine, without undue experimentation, optimal parameters for *in vivo* therapy such as dosages, timing, and methods of administration. What is provided is thus the idea for an invention, and the invitation to experiment to implement this invention, not the invention itself. Applicants rebuke that the dosage and timing of administration of a pharmaceutical composition (i.e., for *in vivo* therapy) must always be individually determined and therefore routine in the practice of the relevant art, and submit the Benet et al. reference (Exhibit C) for support of this argument. However, this argument is not found to be persuasive. Even Benet et al. notes that "to use the data that are presented, one must understand clearance concepts and their application for the computation of drug-dosage regimens. One must also

know average values of clearance, as well as some measures of the extent and kinetics of drug absorption and distribution." Accordingly, because such values are not provided by the instant application, undue experimentation would be required of the skilled artisan to first determine these values in order *then* determine optimal dosages, timing and methods of administration and to thus practice the invention as recited in the claims.

With regard to claim 39, even though the claim is drawn to an *in vitro* method for reducing inhibition of a morphogen activity in a neuron, the specification *does not* enable a method whereby the increased morphogen activity results in the neuron's proliferation, growth, and maintenance of the differentiated state. The specification is enabling for methods of reducing dendritic retraction *in vitro* (or conversely for reducing inhibition of dendritic growth *in vitro*), however, no guidance is provided for methods resulting in neuronal proliferation, growth, and maintenance in the differentiated state. While the instant disclosure provides guidance for *in vitro* methods of reducing dendritic retraction, particularly with regard to the five agents recited in claim 39, dendritic growth does not equate to neuronal proliferation, growth, and maintenance. For example, Bruckenstein and Higgins (*Developmental Biology*, 1988, 128(2): 337-348) report that serum-derived factors which affected dendritic sprouting in sympathetic neurons in culture had little effect on axonal outgrowth or neuron proliferation.

Therefore, due to the large quantity of experimentation necessary to practice *in vivo* methods and particular *in vitro* methods, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the

same, the complex nature of the invention, and the unpredictability of the effects of administering a molecule to a subject, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The rejection of claims 1-2, 5-8, 11, 16-19, 22, 25, and 33-37 under 35 U.S.C. 112, first paragraph (written description), is maintained for reasons of record set forth at pages 10-13 of the previous office action of 13 May 2003 and at pages 15-17 of the office action of 26 July 2004.

Applicants assert on page 9 of the response filed 27 December 2005 that the claims have been amended to more particularly describe what they consider to be the claims invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Contrary to Applicant's assertion that the claims more particularly describe the invention, the claims still recite genera of molecules such as a neuropoietic cytokine antagonist, a retinoid antagonist, a cAMP-dependent messenger pathway inhibitor, or a protein kinase A inhibitor. And, as stated in the previous office action, in addition to being genera of molecules, these agents are genera that are defined not by their structures but by their activity. Therefore, only a specific molecule (such as an anit-gp130 antibody, PI-PLC, and an anti-LIF antibody, for example), but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The rejection of claim 35 under 35 U.S.C. 112, second paragraph, as set forth at page 15 ¶40 of the previous office action (13 May 2005) as being unclear as to the meaning of the phrase "activity of OP-1" is maintained for reasons of record.

New Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

Claims 1-2, 5, 8, 11-12, 19, 22, 25-26, and 33-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2, 5, 8, 11-12, 19, 22, 25-26, and 33-40 recite the "inhibition of the morphogen activity in a neuron *in vitro*" "wherein the morphogen activity is endogenous" and also "overcoming inhibition of growth-promoting effects of endogenous morphogens *in vitro*". It would not be expected that morphogens or morphogen activity would be endogenously expressed in cultured neurons. Accordingly, if the morphogens or their activities are not present *in vitro*, it would not be possible to inhibit their effects or activities consistent with the recited method. The metes and bounds of the claims thus cannot be determined.

Regarding claim 41, the acronym "OP-1" renders the claim vague and indefinite. Abbrevations should be spelled out for clarity.

Conclusion

Claims 1-2, 5-8, 11-12, 16-19, 22, 25-26, and 33-41 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kimberly Ballard, Ph.D.
Art Unit 1649
March 17, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER